

Serial No: 09/526,193

Filed: 15 March 2000

In the Specification:

✓
Please amend the paragraph at page ¹⁶~~15~~, lines 10-16, as follows:

I₁
Figs. 1A (depicted as Fig. 1A-1 carrying over to Fig. 1A-2, collectively Fig. 1A) and 1B (TD-1 and TD-2). Square and circle symbols represent males and females, respectively. Diagonal lines are placed through the symbols of all deceased individuals. A shaded symbol on both alleles indicates the probands with Tangier Disease. Individuals with half shaded symbols have HDL-C levels at or below the 10th percentile for age and sex, while those with quarter shaded symbols have HDL-C between the 11th and 20th percentiles.

✓
Please amend the paragraph at page 22, lines 11-12, as follows:

I₂
~~Fig. 10 shows~~ Figs. 10A and 10B (collectively Fig. 10) show the 5' and 3' nucleotide sequences suitable for use as 5' and 3' PCR primers, respectively, for the amplification of the indicated ABC1 exon.

✓
Please amend the paragraph at page 22, lines 13-14, as follows:

I₃
~~Fig. 11 shows~~ Figs. 11A - 11D (collectively Fig. 11) show a summary of alterations found in ABC1, including sequencing errors, mutations, and polymorphisms.

✓
Please amend the paragraph at page 22, lines 15-24, as follows:

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I4
~~Fig. 12 shows Figs 12A - 12P (collectively Fig. 12) show~~ a series of genomic contigs (SEQ ID NOS. 14-29) containing the ABC1 promoter (SEQ ID NO: 14), as well as exons 1-49 (and flanking intronic sequence) of ABC1. The exons (capitalized letters) are found in the contigs as follows: SEQ ID NO: 14-exon 1; SEQ ID NO: 15-exon 2; SEQ ID NO: 16-exon 3; SEQ ID NO: 17-exon 4; SEQ ID NO: 18-exon 5; SEQ ID NO: 19-exon 6; SEQ ID NO: 20-exons 7 and 8; SEQ ID NO: 21-exons 9 through 22; SEQ ID NO: 22-exons 23 through 28; SEQ ID NO: 23-exon 29; SEQ ID NO: 24-exons 30 and 31; SEQ ID NO: 25-exon 32; SEQ ID NO: 26-exons 33 through 36; SEQ ID NO: 27-exons 37 through 41; SEQ ID NO: 28-exons 42-45; SEQ ID NO: 29-exons 46-49.

✓
Please amend the paragraph at page 23, lines 11-15, as follows:

I5
~~Fig. 16 Figs. 16A and 16B (collectively Fig. 16) show~~ a summary of locations of consensus transcription factor binding sites in the human ABC1 promoter (nucleotides 1-8238 of SEQ ID NO: 14). The abbreviations are as follows: PPRE=peroxisome proliferator-activated receptor. SRE=steroid response element-binding protein site. ROR=RAR-related orphan receptor.

✓
Please amend the paragraph at page 49, lines 3-23, as follows:

I6
Phosphorothioate ~~antisense~~ antisense oligonucleotides were designed to be complementary to the regions of the cDNA near newly discovered translation start site. AN-6 and AN-7 both overlap the initiator methionine codon; this site is in the middle of oligonucleotide AN-6. AN-8 is

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Cont.

complementary to the very 5' end of the ABC1 cDNA. Antisense oligonucleotide AN-1 is complementary to the region of the ABC1 cDNA corresponding to the site identified as the ABC1 initiator methionine in AJ012376. Fig. 7C shows that antisense oligonucleotide AN-6 interferes with cellular cholesterol efflux in normal fibroblasts to the same extent as does antisense oligonucleotide AN-1. Transfection with either of these antisense oligonucleotides results in a decrease in cellular cholesterol efflux almost as severe as that seen in FHA cells. In general, antisense oligonucleotides complementary to coding sequences, especially near the 5' end of a gene's coding sequence, are expected to be more effective in decreasing the effective amount of transcript than are oligonucleotides directed to more 3' sequences or to non-coding sequences. The observation that AN-6 depresses cellular cholesterol efflux as effectively as AN-1 implies that both of these oligonucleotides are complementary to ABC1 coding sequences, and that the amino terminal 60 amino acids are likely to be contained in ABC1 protein. In contrast, the ineffectiveness of AN-8 shows that it is likely to be outside the protein coding region of the transcript, as predicted by presence of an in-frame stop codon between the initiator methionine and the region targeted by AN-8.
